



PATENT  
514413-3563

*Handwritten initials and date: 1/13/00*

**UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant(s) : Haaf et al.  
Serial No. : 09/167,351  
For : COMBINATORIAL PREPARATIONS OF  
PHOSPHORUS-CONTAINING ACTIVE  
COMPOUNDS AND INTERMEDIATES BY  
SOLID PHASE SYNTHESIS  
Filed : October 7, 1998  
Examiner : T. C. McCarthy III, Ph.D.  
Art Unit : 1618

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New York, NY 10151

I hereby certify that this correspondence is being deposited with  
the United States Postal Service as first class mail in an envelope  
addressed to: Hon. Commissioner of Patents and Trademarks  
Washington, DC 20231, on January 10, 2000.

Barbara Z. Morrissey, Reg. No.41,205

Name of Applicant, Assignee or Registered Representative

*Handwritten signature: Barbara Z. Morrissey*  
Signature

January 10, 2000

Date of Signature

**RESPONSE**

Assistant Commissioner for Patents  
Washington, D.C. 20231

Dear Sir:

This is in response to the Office Action mailed November 8, 1999 setting a thirty  
(30) day period for response, with the term of reply extended one month (i.e. from December 8,  
1999 to January 8, 2000). Since January 8, 2000 is a Saturday, this response is timely filed on  
Monday, January 10, 2000.

An election under 35 U.S.C. § 121 has been required to the subject matter of:

- Group (I) Claims 1 to 9, drawn to a process for preparing compounds, classified in class 436, subclass 523;
- Group (II) Claim 10, drawn to a compound, classified in class 514, subclass 42;
- Group (III) Claim 11, drawn to a library, classified in class 514, subclass 42;
- Group (IV) Claims 12 and 13, drawn to a library, classified in class 514, subclass 42;
- Group (V) Claim 14, drawn to an assay, classified in class 435, subclass 7.1+ (depending on the compound and assay); and
- Group (VI) Claim 15, drawn to an assay, classified in class 435, subclass 7.1+ (depending on the compound and assay).

In response to the restriction requirement, Applicants provisionally elect **Group I** for further prosecution in this application encompassing claims 1 to 9 drawn to a process for preparing compounds.

This election is made *with traverse* and is made without prejudice to Applicants' right to file divisional applications directed to the non-elected subject matter. It is respectfully requested that the restriction requirement be favorably reconsidered and withdrawn.

The Office Action further requires an election of species (if Applicants elect the claims of Group I) with respect to the following patentably distinct species: compounds, resins and process for preparing the compounds. Applicants elect the following species for searching:

1. Polymer resin is polystyrene resin (200-400 mesh, 1.23 mmol of OH per gram of resin)(see Example 1);
2. Linker is the Wang-linker (see Example 1); and
3. The process is as follows:
  - a) preparation of compound (IVa) as defined in Example 2,
  - b) reaction with 4-nitrobenzaldehyde as defined in Example 3, first paragraph, and
  - c) delinker reaction with TFA to yield final product (I) as defined in Example 3.

The elected process is covered by claims 1 to 9.

The requirement for an election of species is also respectfully traversed since the species are related to one another. It is noted that claim 1 is deemed generic and it is Applicants understanding that upon the allowance of a generic claim, Applicants will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all of the limitations of an allowed generic claim as provided by 37 C.F.R. 1.141.

It is respectfully noted that it would not be an undue burden on the Patent Office to search all the pending claims in a single application. Accordingly, it is submitted that the restriction requirement is improper and should be reconsidered and withdrawn.

The MPEP lists two criteria for a proper restriction requirement. First, the inventions must be independent or distinct. MPEP § 803. Second, searching the additional inventions must constitute an undue burden on the examiner if restriction is not required. *Id.* The MPEP directs the search and examination of an entire application “[i]f the search and examination of an entire application can be made without serious burden, ...even though it includes claims to distinct or independent inventions.” *Id.*

The Office Action states that the subject matter of Groups I, II, III, IV, V and VI are distinct inventions which have acquired separate status in the art due to their recognized divergent subject matter. In particular, it is alleged that the processes of Group I to make a compound are different from those required to assay a compound for activity, and that the processes are practiced for different purposes. Furthermore, it is stated that the individual compounds of Group II and the libraries of the compounds of Groups III and IV are by definition distinct, because by definition a library is two or more compounds and is therefore distinct from a single compound. It is also stated that the inventions of Groups III and IV are different from one another, as the libraries of compounds have different structures and functionalities, and the

art reading on one library would not read on the other. Further, the Office Action states that Groups VI and VII for the assays are different from one another in that the assay of invention of Group VI is practiced using a library of compounds that contain different structures/functionalities than the library used to practice the Group VII.

The present invention is directed to solid phase processes for the systematic preparation of chemical compounds from the group of the phosphonous and phosphinic acids and/or derivatives thereof and the corresponding substance libraries which can be employed for test purposes, in particular, testing for biological activity. The processes for preparing the compounds of the present invention are performed by reacting a resin linker adduct in the presence of a suitable catalyst with a phosphinate to yield a resin bound compound from which the compounds of the present invention can be cleaved. The invention also provides for the intermediate steps, the resin-linked intermediate compounds and the substance libraries obtained therefrom.

Applicants respectfully submit that the claims of Groups I to VI should not be subject to restriction as they are all related and are directed to the same inventive concept. The processes of Group I are performed using the intermediate compounds claimed in Group II and are used to produce the library of compounds claimed in Groups III and IV. The assays of Groups V and VI are used to test the compound of the libraries claimed in Group IV, which are in turn based on the compounds produced by the processes claimed in Group I. Similarly, the library of compounds in Group III relate to the intermediate compounds used in the processes of Group I. Therefore, all of the processes, compounds and assays are all related to the same inventive concept.

It is also respectfully submitted that the claims in Groups I to VI may be searched and examined together without serious burden, as they all relate to the processes claimed in Group I. For example, the compounds claimed in Group II and the compound library of Group III are drawn to the compounds of the processes of Group I. In particular, the compounds of formulae (II), (IV), (IV'), (V), (VI), (VI'), (VII), (VII'), (VIII), (VIII') and (IX) are all intermediates of the process for preparing compounds of formula (I). Additionally, they are all resin polymer bound compounds and with the exception of starting compound (II), these compounds always have a phosphorus containing functional group. Searching the process claims of Group I would necessarily overlap and include a search of the individual compounds and intermediates of Groups II and III. Similarly, searching the process claims of Group I for the processes using the intermediates of Groups II and III, which are linked to a resin polymer to prepare chemical compounds of formula (I), would necessarily overlap and include a search of the compounds and library of Group IV.

In view of the similarity among claims 1 to 15, it is submitted that a search of the prior art when examining the claims of Group I would, at the same time, result in a search of prior art for use in examining all the remaining claims of the application.

As acknowledged in the Office Action on page 2, the claims in Group I and Groups II, III, and IV are related as process of making and product made. The Office Action goes on to state that inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different products, or (2) that the product as claimed can be made by another and materially different process (MPEP 806.05(f)). The Office Action claims that in the instant case, the products can be made using any

number of known synthesis methods (i.e., solid phase synthesis using light-generated reagents, classical serial synthesis, etc.).

Applicants respectfully assert that the inventions of Groups I to VI are related and that the requirements of the two-part test are not fulfilled. According to part (1) of the test, the inventions are distinct if the process can be used to make other and materially different products. However, the compounds of claim 10 are intermediates of the claimed processes, and per se, the process cannot be used to make other and materially different products.

Further, according to the second part of the test, the inventions are distinct if the products can be made by another and materially different process. The Office Action states that in the instant case, the product can be made using any number of known synthesis methods (i.e. solid phase synthesis using light-generated reagents, classical serial synthesis, etc.). (Office Action, page 2.)

Applicants respectfully assert that the second part of the test for distinctiveness has not been met. First, Applicants contend that the claimed method is a solid phase synthesis and covers light-generated reagent methods for linking scaffolding to resin polymers. Therefore, the reference to "solid phase synthesis" in the Office Action does not distinguish it from the solid phase methods included in the process as claimed.

Secondly, with respect to the introduction of the phosphorus functional group and modifications thereon as defined in claim 1, the Office Action is silent as to the problems of linking compounds containing phosphorus functional groups to resin polymers. It is not clear whether or not there is a workable route for preparing compounds of formulae (IV), (IV'), (V), (VI), (VI'), (VII), (VII'), (VIII), (VIII') and (IX), without preparing the resin polymer bound compound of formula (II) first and introducing the phosphorus functional group thereafter by

reacting with the compounds of formula (III). The Office Action does not cite any reference or teaching which makes this assumption possible. In evaluating other possible methods, it should be considered that many linker systems would react with the phosphorus functional groups producing an undesirable linkage of phosphorus to the polymer resin, or would interfere with the desired linkage reaction.

For the foregoing reasons, the restriction requirement should be withdrawn with respect to the intermediate and their libraries of Groups II and III, as they relate to the processes claimed in Group I.

With respect to the claim of Group IV directed to the compounds of formula (I), the access to libraries of compounds of formula (I) is assumed to be possible through other methods, either in principle or in theory. The issue has not been addressed, however, as to whether libraries obtainable through the process of claim 1 have already been produced by other methods. Similarly, this applies to the method claims of Groups V and VI. Applicants assert that if the libraries of compounds are novel, the methods of use of those compounds should also be examined together in one application.

Further, as acknowledged in the Office Action, the claims of Group II and Groups V and VI are related as product and process of use. It is noted that the Office Action refers to Groups VI and VII, which are believed to be the Groups V and VI directed to claims 14 and 15, respectively. Even though the compounds of Group II are distinct chemical entities having chemical activities to be determined by the assays of Groups V and VI, they are directly related to one another and as such, should be examined in the same application. Therefore, the Applicants maintain that a search of the invention of Group II would substantially overlap with the searches for Groups V and VI.

One of skill in the art would appreciate that the processes of the claims in Group I would utilized the compounds of the invention in Groups II to IV, and that the compounds produced by the processes of Group I may be used to practice the various methods of Groups V and VI. Thus, it is respectfully asserted that, at a minimum, the claims of Groups I, II, III and IV should be joined together, since the Group I search would encompass a search and examination of the compounds claimed in Groups II through IV.

If the restriction requirement is maintained, it is submitted that duplicate searching of the various Groups in separate divisional applications would be quite inefficient to the operation of the Patent and Trademark Office. It would therefore be most beneficial for both efficiency and cost savings to the Applicant, as well as the PTO, for this case to proceed without restriction.

Furthermore, it is likely that the same Examiner would be in charge of the divisional cases, but since these divisional applications would be examined at a much later date the Examiner will have to conduct a duplicate, redundant search at the time she examines the divisional cases. Alternatively, if a different Examiner is assigned to the divisional applications, a significant loss of PTO efficiency would be incurred as a results of the examination of divisional cases.

It is respectfully urged that restricting the claims in the manner suggested in the restriction requirement constitutes an undue burden to Applicants. If followed, the restriction requirement would require Applicants to file a number of additional applications. The cost of prosecuting and maintaining additional patents is unreasonable in view of the fact that the application as filed includes claims that are all related to one another. Further, under GATT, the period of exclusivity for any patents which issue from these divisional applications is greatly



reduced. In addition, the public is inconvenienced as they will not know whether or not Applicants will file divisional applications to the remaining subject matter. Accordingly, the public will not know if they can practice the remaining invention without infringing future patent applications.

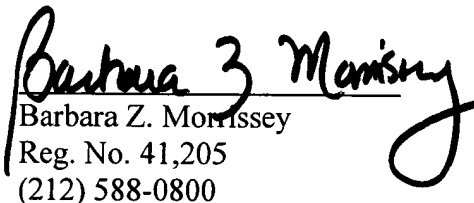
In view of the foregoing, Applicants respectfully request that the restriction requirement as to claims 1 to 15 be reconsidered and withdrawn and respectfully submit that all of the claims should properly be examined in one application. Early and favorable examination of claims 1 to 15 is respectfully requested.

Applicants have not amended the wording of the claims due to the fact that the claims cover the possible variants that the combinatorial synthesis methods can produce and thus it is difficult to simplify the claims without losing accuracy and precision. The working examples in the specification illustrate the process in specific detail and they assist one in more easily understanding the claims. Nonetheless, Applicants welcome any suggestions of the Examiner to modify the claim language.

This paper is being filed with a Request for one month Extension of Time, along with the requisite fee for the extension of time. If any additional fee is determined to be due, the Assistant Commissioner is authorized to charge such fee, or credit any overpayment, to Deposit Account No. 50-0320.

Respectfully submitted,  
FROMMER LAWRENCE & HAUG LLP

By:

  
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